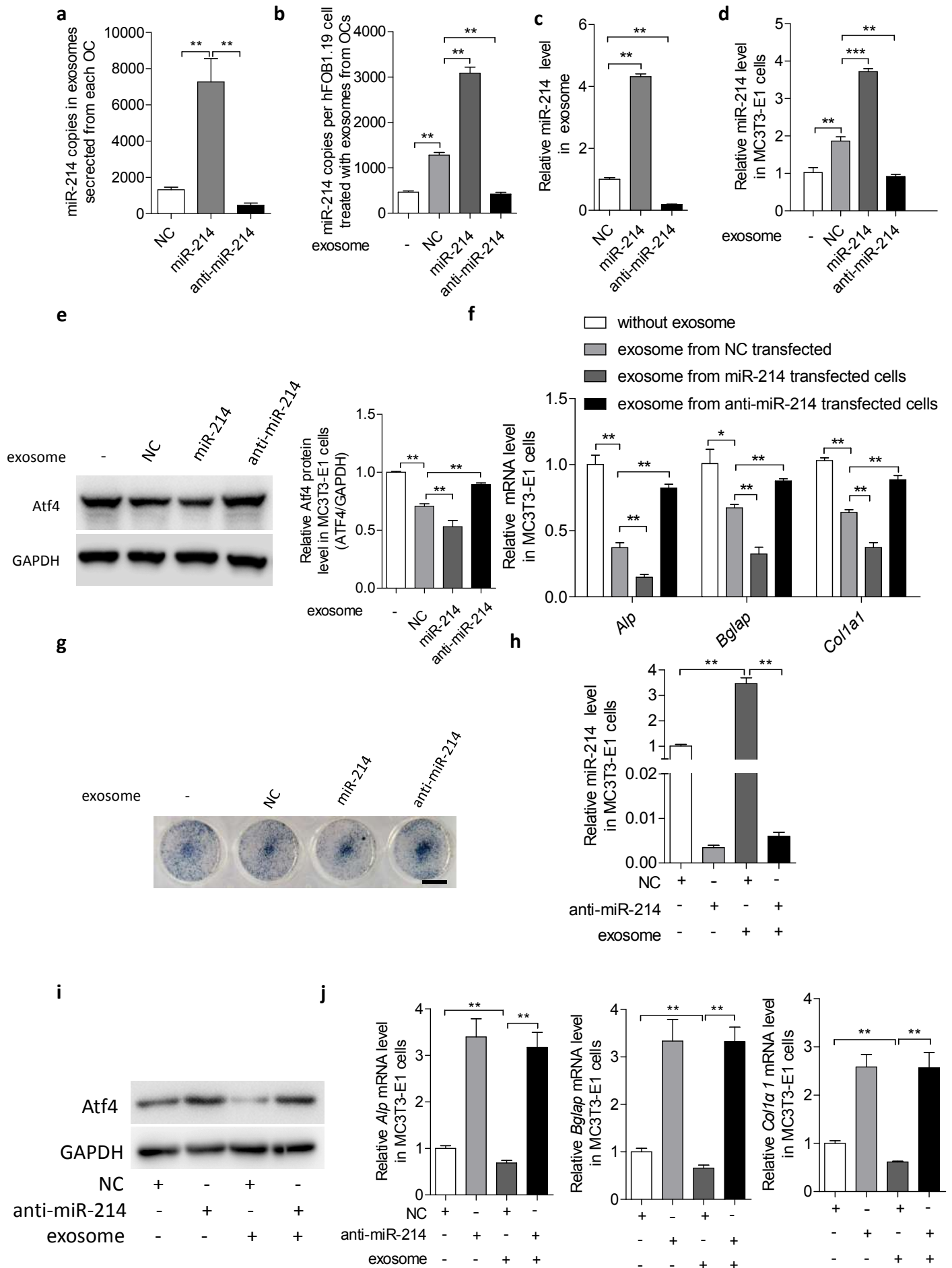
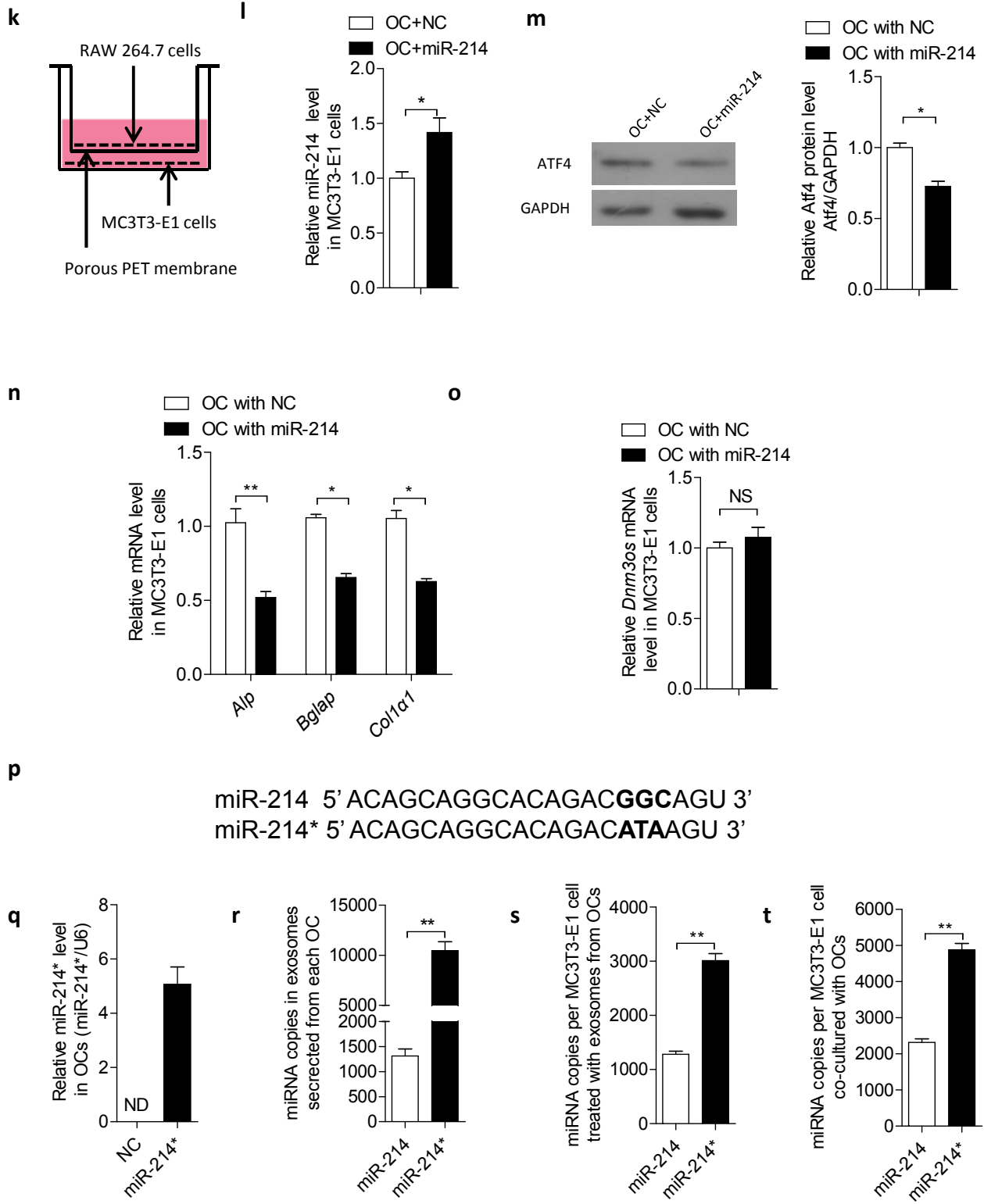


**Supplementary Figure 2**



## Supplementary Figure 2



**Supplementary Figure 2. miR-214 transfer from osteoclasts to osteoblasts to inhibit osteoblast function.**

(a) miR-214 copies in exosomes secreted from each osteoclast cell were analyzed by qRT-PCR and calculated according to the standard curves. (b) miR-214 copies in each hFOB1.19 cell were analyzed by qRT-PCR and calculated according to the standard curves. hFOB1.19 cells ( $10^5$ ) were incubated with exosomes secreted from osteoclasts ( $10^6$ ) transfected with 300 pmol NC, miR-214 or anti-miR-214. (c) QRT-PCR analysis of miR-214 levels in exosomes from the medium of RAW 264.7 cells. These cells were transfected with NC (negative control), miR-214 (miR-214 mimics) or anti-miR-214 (the inhibitor of miR-214) for 2 days under the treatment with RANKL. MiR-214 levels were normalized to *RNU6*. (d) miR-214 level in MC3T3-E1 cells was analyzed by qRT-PCR after incubation for 2 days with or without exosomes secreted (5  $\mu$ g/ml) from RAW 264.7 cells transfected with NC, miR-214 or anti-miR-214 for 2 days under the treatment with RANKL. (e) Atf4 protein levels in MC3T3-E1 cells were analyzed by western blot after incubation with or without exosomes and were normalized to GAPDH. (f) *Alp*, *Bglap* and *Col1 $\alpha$ 1* mRNA levels in MC3T3-E1 cells were analyzed by qRT-PCR after incubation with or without exosomes. The transcripts levels were normalized to *Gapdh*. (g) Representative images of Alp staining of osteoblasts after incubation with or without exosomes for 6 days. (h) miR-214 level in MC3T3-E1 cells was analyzed by qRT-PCR after transfection with anti-miR-214 or NC, and incubation with or without exosomes (5  $\mu$ g/ml) secreted from osteoclasts. (i) Atf4 protein levels in MC3T3-E1 cells were analyzed by western blot in those groups and were normalized to GAPDH. (j) *Alp*, *Bglap* and *Col1 $\alpha$ 1* mRNA levels in MC3T3-E1 cells were analyzed by qRT-PCR in those groups. The transcripts levels were normalized to *Gapdh*.

(k) *In vitro* co-culture system was used where RANKL - induced RAW 264.7 cells were seeded in the top compartment, which was separated by a 0.4  $\mu$ m porous membrane from MC3T3-E1 cells that were cultured in the bottom compartment. (l) The change of miR-214 levels in MC3T3-E1 cells after co-cultured with RANKL (50 ng/ml)-induced RAW 264.7 cells transfected with miR-214 mimics or NC for 2 days. (m) The change of Atf4 protein level in MC3T3-E1 cells after co-cultured with RANKL-induced RAW 264.7 cells transfected with miR-214 mimics or NC. (n) The changes of *Alp*, *Bglap*, *Col1 $\alpha$ 1* mRNA levels in MC3T3-E1 cells after co-cultured with OC transfected with miR-214 mimics or NC. Their levels were analyzed by qRT-PCR and normalized to *Gapdh*. (o) The change of *Dnm3os* mRNA level in MC3T3-E1 cells after co-cultured with OC transfected with miR-214 mimics or NC. *Dnm3os* mRNA level was analyzed by qRT-PCR and normalized to *Gapdh*. (p) The sequences of miR-214 and miR-214\*. (q) Osteoclasts were transfected with miR-214\* or not, collected after 48 h, then the levels of miR-214\* were analyzed by miR-214\* specific probe. (r) miR-214 and miR-214\* copies in exosomes secreted from each osteoclast were analyzed by qRT-PCR and calculated according to the standard curves. Osteoclasts ( $10^5$ ) were transfected with 60 pmol miR-214\*. (s) miR-214 and miR-214\* copies in each MC3T3-E1 cell were analyzed by qRT-PCR and calculated according to the standard curves. MC3T3-E1 cells ( $2 \times 10^5$ ) were incubated with exosomes secreted from osteoclasts ( $10^5$ ) transfected with 60 pmol miR-214\*. (t) miR-214 and miR-214\* copies in each osteoblasts were analyzed by qRT-PCR and calculated according to the standard curves. MC3T3-E1 cells ( $2 \times 10^5$ ) were co-cultured with osteoclasts ( $10^5$ ) transfected with 60 pmol miR-214\*. The data represent the mean  $\pm$  SEM of three independent experiments. \* $P < 0.05$ , \*\* $P < 0.01$ .